THE AQUO AMMONO PHOSPHORIC ACIDS

I. PREPARATION OF THE PHENYL ESTERS OF AMIDO- AND DIAMIDOPHOSPHORIC ACIDS AND THEIR N-SUBSTITUTED DERIVATIVES

II. N-SUBSTITUTED DERIVATIVES OF PHOSPHORYL AND THIOPHOSPHORYL TRIAMIDE AS HYDROGEN BONDING AGENTS

BY

ARTHUR DOCK FON TOY

B.S., University of Illinois, 1939

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AN ABSTRACT OF A THESIS

SUBMITTED IN PARTIAL FULFILLMENT OF THE REQUIREMENTS FOR THE DEGREE OF DOCTOR OF PHILOSOPHY IN CHEMISTRY IN THE GRADUATE SCHOOL OF THE UNIVERSITY OF ILLINOIS, 1942

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I. PREPARATION OF THE PHENYL ESTERS OF AMIDO- AND DIAMIDOPHOSPHORIC ACIDS AND THEIR N-SUBSTITUTED DERIVATIVES

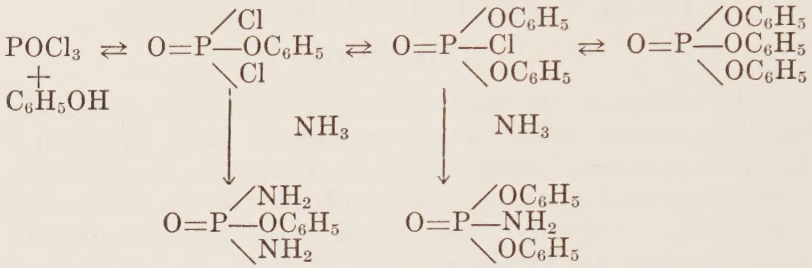
A. Introduction

In extending the studies carried out in this laboratory on the sulfamic acids, it was considered to be of distinct theoretical and technical interest to undertake an investigation of the analogous nitrogen derivatives of the phosphorus compounds, especially those which might appropriately be termed, from the Franklin[1] point of view, the phosphamic acids. The synthesis of these acids necessitated the preparation of the intermediate phenyl esters in considerable quantities. Stokes[3] had previously prepared these esters in poor yields by the treatment of the respective chlorophosphates with aqueous or alcoholic ammonia. This method was found to be unsatisfactory because the preparation of the chlorophosphates involves long heating and tedious fractionation. Therefore it seemed desirable to develop an easier and more practical method for the preparation of the phenyl esters of these aquo ammono phosphoric acids.

King and Nicholson[2] have described the synthesis of the phenylphosphoric acids by the hydrolysis of the product obtained when molar proportions of phenol dissolved in pyridine are allowed to react with phosphoryl chloride. The latter reaction takes place quickly without the necessity of prolonged heating. It was considered quite probable that ammonolysis and aminolysis of the product of interaction of phosphoryl chloride and phenol in the presence of pyridine would afford a simple method for preparing the amides as well as the N-substituted amides of the alkyl and aryl phosphoric acids. A more extended study of this procedure was therefore undertaken in order to adapt it to the preparation of phenyl diamido- and diphenyl amidophosphates and their N-substituted derivatives.

B. Discussion of the Experimental Results

The experimental results indicate that a complex equilibrium is established when phosphoryl chloride and phenol react in the presence of pyridine.



Pyridine not only effects removal of hydrogen chloride but also the stabilization of the intermediate chlorophosphates presumably with the formation of pyridine complexes. Rise in temperature, increase in the molar ratios both of pyridine and of phenol to phosphoryl chloride, favor a shift in equilibrium to the right. It was found best to use chloroform as solvent and diluent for the reaction (a) since it permitted more careful temperature control and (b) because the reaction product was found to be completely soluble in it. Ammonolysis of the resulting product may be effected by aqueous or gaseous ammonia, but liquid ammonia was found not only to be most convenient, but also to give higher yields of the products. For best results, a $POCl_3$:C_6H_5OH:C_5H_5N molar ratio of 1:0.77:3 should be used when phenyl diamidophosphate is desired, while the ratio of 1:2:3 is recommended when the diphenyl amidophosphate is desired. Though a mixture is always obtained, the two can be separated easily by hot chloroform which dissovles readily the diphenyl amidophosphate, while the diamidophosphate is only very slightly soluble.

This method was extended to aminolytic reactions for the preparation of the N-substituted derivatives. For purposes of identification the N-substituted derivatives were first prepared by the direct action of the phenyl chlorophosphates on the amines. The compounds prepared were the phenyl di-

(methylamido)-, di-(cyclohexylamido)-, di-(anilido)- and di-(morpholido)-phosphates, and the diphenyl methylamido-, morpholido-, cyclohexylamido-, and anilidophosphates.

The aminolysis of the $POCl_3$-C_6H_5OH-C_5H_5N mixture as a means for preparing these compounds was found to be only partially successful, due to the fact that mixtures are always obtained. For the monophenyl N-substituted derivatives a $POCl_3$:C_6H_5OH:C_5H_5N ratio of 1:0.77:3 was employed; for the diphenyl derivatives a ratio of 1:2:3 was used. Phenyl di-(methylamido)-phosphate was obtained in good yield because it is less soluble in cold carbon tetrachloride than the by-product diphenyl methylamidophosphate. The phenyl di-(morpholido)-phosphate is soluble in water, permitting its separation from the water insoluble by-products. In case of the other compounds, suitable solvents for the separation of monophenyl derivatives from the diphenyl were not found.

This procedure is even less successful where the diphenyl N-substituted phosphates are desired. Triphenyl phosphate is always obtained as a by-product. Substitution of amine for ammonia results in products which closely resemble the triphenyl phosphate in solubilities making separation difficult, if not impossible.

C. Bibliography

1. Franklin, The Nitrogen System of Compounds. Reinhold Pub. Corp. N. Y. 1935.
2. King and Nicholson, Biochem. J., **33**, 1182 (1939).
3. Stokes, Am. Chem. J., **15**, 198 (1893); **16**, 123 (1894).

II. N-SUBSTITUTED DERIVATIVES OF PHOSPHORYL AND THIOPHOSPHORYL TRIAMIDE AS HYDROGEN BONDING AGENTS

A. Introduction

The esters of phosphoric acids have been used widely as plasticizers for various polymeric substances which contain active acceptor atoms. Hydrogen bonding is considered to play an important role for it is assumed that the oxygen atoms in the phosporic acid esters serve as donor atoms in bonding to active hydrogen atoms. Copley, Zellhoefer, and Marvel[1,2]

have shown that the extraordinary solubility of CH_2Cl_2 in a series of phosphoric acid esters may be explained on the basis of the hydrogen bond theory.

The analogous N-alkyl and N-aryl substituted derivatives of phosphoryl triamide, $PO(NH_2)_3$, may be looked upon as ammono esters. Theoretically, the ammono phosphoric acid esters should serve as hydrogen bonding agents because of the presence of both oxygen and nitrogen atoms which may be capable of acting as donor atoms.

Donor molecules have been found to exhibit extraordinarily high solubility in such solvents as chloroform which contains a labile acceptor hydrogen atom. On the other hand solubility of these same materials in solvents such as carbon tetrachloride is considerable less due to the absence of an active hydrogen atom in carbon tetrachloride. In order to determine the effect of structure upon hydrogen bonding ability, a series of N-substituted phosphoryl and thiophosphoryl triamides were prepared and these together with related compounds were investigated for their solubility in chloroform and in carbon tetrachloride at 25°.

B. Discussion of the Experimental Results

The preparation of the N-substituted phosphoryl triamides was simplified and improved by making use of a solution of the phosphoryl chloride-pyridine complex in chloroform. Aminolysis of this product was found to proceed smoothly and to give the desired compound in better yields than any method heretofore suggested.

The marked difference in solubility of the N-substituted phosphoryl triamides in chloroform and in carbon tetrachloride is especially striking in the case of the morpholine derivatives in which oxygen atoms are located in peripheral positions in the ring and the nitrogen atoms are devoid of hydrogen. The derivatives of aniline and amines of similar structures are more soluble in chloroform than in carbon tetrachloride, but the solubility in chloroform is very low in every case. This may be due to the fact that the nitrogen atom is

attached in each case directly to a phenyl ring which permits the pair of free electrons on the nitrogen to resonate with the electrons in the double bonds of the phenyl ring. Thus the availability of nitrogen as a donor atom is decreased. This hypothesis is substantiated by the observation that elimination of resonance (a) by reduction of the ring, as in the case of the cyclohexylamine derivative, or (b) by separating the nitrogen from the phenyl group by means of a CH_2 group, as in case of the benzylamine derivative, brings about a great increase in solubility in chloroform. The p-phenetidine derivative, with an ether oxygen attached to the ring, is more soluble in chloroform than the anilide. Presumably the extra oxygen serves as another donor atom, but this increase is not of the same order of magnitude as that observed in the morpholine derivatives where the oxygen atom is in the ring. The difference may be due to the fact that the electrons in the oxygen next to the phenyl ring are in resonance with the electrons in the double bonds in the ring.

Much lower solubility in chloroform is observed in the compounds where the oxygen atom, connected directly to the phosphorus atom, is replaced by a sulfur atom which is generally assumed to have no donor ability.

C. Bibliography

1. Copley, Zellhoefer, and Marvel, J. Am. Chem. Soc., **60**, 2666 (1938).
2. Copley, Zellhoefer, and Marvel, **ibid.**, **60**, 2714 (1938).

VITA

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He is a member of the following scientific and honorary societies: American Chemical Society, American Association for the Advancement of Science, Sigma Xi, Phi Lambda Upsilon, Phi Kappa Epsilon, and Phi Beta Kappa.